

RIGHT TRISEGMENTECTOMY FOR HEPATIC NEOPLASMS

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RIGHT trisegmentectomy or extended right hepatic lobectomy involves removal of the true right lobe of the liver plus the medial segment of the left lobe, leaving behind the variable 10 to 25 per cent of hepatic tissue that lies to the left of the falciform ligament. The operation was first performed almost 30 years ago by Wangenstein (27), Lortat-Jacob and Robert (17) and Quattlebaum (22), but until recently, its forbidding mortality prevented wide use.

In 1975, we described in detail a safe technique of right trisegmentectomy (23). We report here an evaluation of the early and later results in 30 patients who had this operation for 26 primary or metastatic malignant tumors and for four nonmalignant lesions. In addition, a modification from our original technique will be mentioned that has been particularly useful for bulky superior and posterior hepatic tumors including those that invade the diaphragm.

METHODS

Thirty patients had trisegmentectomy. Nine pediatric patients had a mean age of 10.3 ± 4.9 S.D. years, a range of two to 16 years. Five were girls and four were boys. The 21 adults had a mean age of 51.1 ± 16.2 S.D. years, a range of 19 to 74 years. Excluding the three adult women with benign hepatic lesions, the average age was 55.1 ± 13.4 S.D. years. Thirteen of the adults were women and eight were men. Many of the patients who were referred for consideration of transplantation had been judged at other hospitals to have unresectable tumors. Fifteen of the patients had undergone at least one exploratory laparotomy before referral.

The histopathologic diagnoses are listed in Table I. There were four nonmalignant lesions, three adenomas and one focal nodular hyper-

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plasia. Three were in adults. One adenoma was in a 16 year old girl.

Hepatomas were the most common of the primary hepatic malignant lesions (Table I). One of these, which was undifferentiated, was thought by some local and consulting pathologists to be a sarcoma; this divided opinion was never reconciled.

The conditions varied with hepatic resection for metastatic lesions. The most common localized hepatic metastases were colorectal in origin (Table II). Resection of the primary colonic or rectal tumor had been done 12 to 18 months earlier. The patient with neuroblastoma had simultaneous trisegmentectomy, right adrenalectomy and excision of a right retroperitoneal mass. Lymph nodes in the portal triad contained neuroblastoma. The tumor was considered Stage IV, by the criteria of Evans and associates (6). The tissue diagnoses in patients with glucagonoma and metastatic squamous cell carcinoma of the cervix were first made from the study of the hepatic specimen. In the first instance, a primary pancreatic tumor could never be found, even at autopsy, and in the second, the uterine cervical primary tumor was later treated with irradiation followed by hysterectomy and pelvic node dissection. The woman with carcinoma of the gallbladder had trisegmentectomy one month after cholecystectomy. A 1.5 centimeter recurrence was found in the fossa of the gallbladder of the resected hepatic specimen. Three of the 30 patients had cirrhosis with one example each of mild, moderate and severe.

SURGICAL TECHNIQUE

Trisegmentectomy was usually performed as described before (23). The principles were dissection and division of the hilar strictures entering the proposed specimen, division and suture closure or ligation of the hepatic veins leaving the specimen and a splitting of the hepatic parenchyma exactly along the intersegmental plane. The remaining lateral segment has been shown by Buerk and collaborators (4) to accommodate

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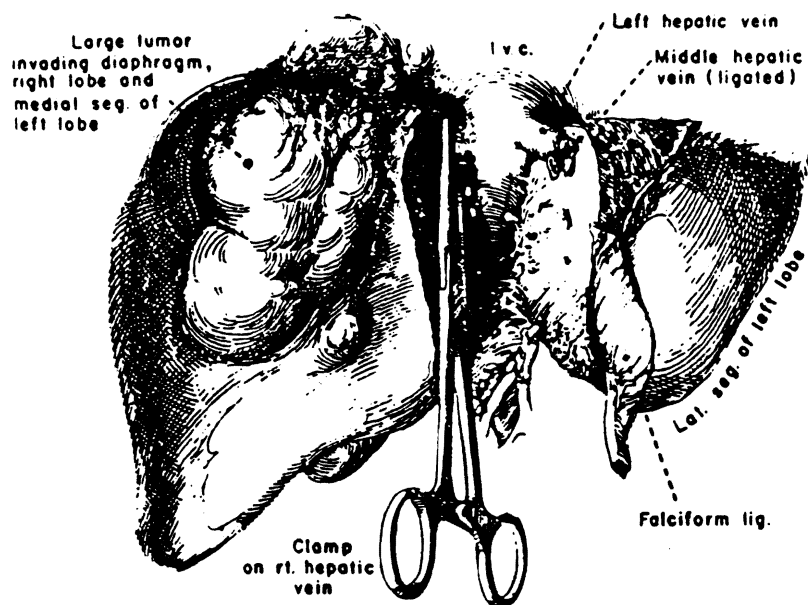


FIG. 1. Control of right hepatic vein from within the liver. I.V.C., Inferior vena cava.

total portal blood flow without an increase in portal pressure.

A modification omitting preliminary outflow control was useful or even essential for bulky tumors that were posteriorly or superiorly located. After ligating the hilar structures, cleavage of the liver was carried out in the plane of the falciform ligament. The right hepatic vein was approached, cross clamped, divided and closed with suture from within the split parenchyma, as illustrated in Figure 1. When tumor had invaded the diaphragm, diaphragmatic excision could be carried out as the last step in excision of the specimen.

In one such patient, it was found at the last moment that the tumor had invaded the vena cava and left hepatic vein. These structures were excised. A reversed vena caval-iliac homograft was used to replace the entire retrohepatic vena cava, and one of the iliac veins was anastomosed to a centrally located hepatic vein of the hepatic fragment (Fig. 2).

Clamps, such as those described by Lin (15) and Storm and Longmire (25) for temporary hemostasis of the raw surface of the liver were not used. Operative transfusions averaged about 2,500 milliliters for adults and less for children. Fresh blood, blood products and clot promoting pharmacologic agents were not used. Massive drainage was provided by leaving part of the incision open and by filling the wound base with soft rubber drains (23).

POSTOPERATIVE CARE

Broad spectrum antibiotics which were begun 12 hours before operation were continued for three or four days. The drains were removed in two to five days, and irrigations of the cavity done once or twice daily were begun with normal saline solution to which antibiotics were sometimes added. The wounds were allowed to heal from the depths. This required several weeks. Filling in of the hepatic fossa by regenerating the liver was a factor in shortening the time of wound healing.

Standard postoperative care was given including prolonged support of ventilation in some instances. Specific methods to prevent or ameliorate hepatic failure were not ordinarily necessary. All of the patients became jaundiced postoperatively with high bilirubin levels of 4 to 30 milligrams per cent. The icterus reached a peak within a few days and receded progressively thereafter in all but one of the operative survivors. Other abnormalities in liver function were equally transient. Rises in serum transaminase levels were almost always minor, indicating that little damage had been inflicted on the residual fragment.

ADJUVANT THERAPY

Nine of the 26 patients with malignant disease received no treatment of the hepatic lesion other than resection. They were 50 to 74 years old, with an average age of 63 years. They declined

TABLE I.—INDICATIONS FOR AND RESULTS AFTER TRISEGMENTECTOMY WITH FOLLOW-UP STUDY TO 1 APRIL, 1979

Diagnosis	No. of patients	Operative death	Later death*	Alive tumor-free	Alive with recurrence
Benign	4	0	0	4 (50, 53, 82, 101)	0
Hepatoma	14	1	3 (12, 19, 33)	7 (66, 41, 21, 13, 6, 3, 2)	3 (7, 9, 21)
Sarcoma	3	0	1 (2)	2 (47, 42)	0
Squamous cell carcinoma, cyst	1	0	1 (4½)	0	0
Cholangiocarcinoma	1	0	1 (47)	0	0
Localized metastases	7	0	3 (13, 18, 18)	2 (52, 9)	2 (41, 6)
Total	30	1	9	15	5

*Later deaths were all due to recurrence.
Figures in parentheses are months.

further treatment or were considered to be too frail to receive it. Some who are still in the early postoperative period may become candidates for delayed chemotherapy. Two patients, one patient with squamous cell carcinoma in a cyst and the other with neuroblastoma, received 3,000 rads local irradiation plus multiple agent chemotherapy.

In 14 other patients, chemotherapy was variable and planned according to the histopathologic diagnosis. Initially, the most common treatment for hepatomas was cyclophosphamide, 5-fluorouracil and vincristine, as described by Holton and co-workers (11). This was followed with adriamycin if necessary for recurrences. The heterogeneity of the constituents, dosages and timing of adjuvant therapeutic protocols precluded conclusions about effectiveness beyond the observation that long term survival was obtained without, as well as with, adjuvant therapeutic treatment.

When used, adjuvant treatment was begun only after recovery from the surgical procedure seemed assured. In most of the patients with localized metastases, the previously used chemotherapy was resumed. The time postoperatively usually ranged from a few days to several weeks. The stage of regeneration was not taken into account. The assumption was made that, once in full motion, the regeneration process would not be halted or seriously inhibited by irradiation or chemotherapy.

RESULTS

Mortality. There was one operative death, 3.3 per cent, out of the 30 patients who underwent resections. This patient was a woman who required a reversed vena caval and iliac homograft to replace the excised left hepatic vein and retrohepatic vena cava. Hepatic venous drainage for the lateral segment was successfully provided (Fig. 2). Her initial course was satisfactory, but after ten days, the serum transaminase concentrations rose to extremely high levels. Hepatic insufficiency developed, and she died 20 days postoperatively. At autopsy, the celiac axis was occluded by fresh thrombosis that may have been initiated by selective arteriography one week preoperatively. The thrombosis was far from the field of operative dissection, and the liver fragment had extensive necrosis.

Morbidity. One of the 30 patients required re-exploration on the first postoperative night to control hemorrhage from the raw liver surface. Four of the 30 patients had abscesses develop in the hepatic fossa or right subhepatic space. These were drained by reopening the drain tracts which had closed prematurely at, or near, the anterior body wall. Two patients required secondary closure of the incisional gaps left for drainage, through which bowel herniation occurred. Minor bile leaks through the drain site were common, but these all closed spontaneously. There were no late complications of the bile duct. Temporary drainage of ascites was severe only in a 19 year

TABLE II.—RESULTS FOR PATIENTS WITH TRISEGMENTECTOMIES FOR METASTASES WITH FOLLOW-UP STUDY TO 1 APRIL, 1979

Diagnosis	Adjuvant chemotherapy	Tumor recurrence by one year	Died	Status now
Carcinoma of the colon	Yes	Yes	18 mos.	Known recurrence, 41 mos. Tumor-free, 9 mos.*
Carcinoma of the rectum	Yes	Yes		
Carcinoma of the colon	No			
Carcinoma of the gallbladder	Yes	Yes	18 mos.	Dying, metastases, 6 mos. Tumor-free, 52 mos.
Glucagonoma, ? pancreas	No	Yes	13 mos.	
Squamous cell carcinoma of the cervix	No	Yes		
Neuroblastoma	Yes	No		

*Choriocarcinoma antigen was 350 nanograms per milliliter before operation and is now normal, <2.5 milligrams.

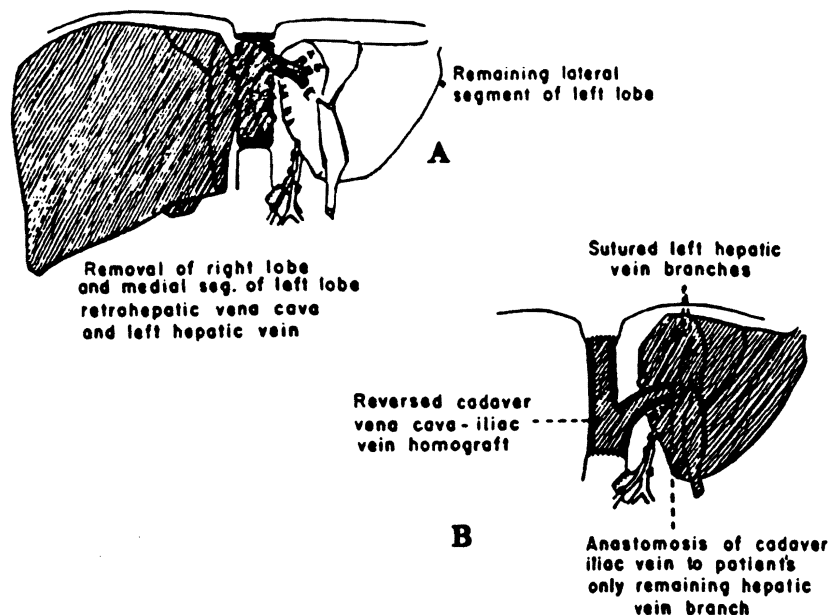


FIG. 2. a and b, Technical management of patient whose intrahepatic vena cava and left hepatic vein were invaded by tumor.

old woman with an unusually small liver fragment (24).

In surviving patients, regeneration, as judged by serial scans, was complete or nearly complete in two or three months, with two exceptions. One patient, in whom about 90 per cent of the liver was excised, never had complete restoration of hepatic mass, although liver function became normal (24). Another patient had an angiosarcoma in a liver made severely cirrhotic by Thorotrast, thorium dioxide, injections 25 years previously. He died more than two months postoperatively with multiple metastases in the fragment. The residual tissue had little evidence of regeneration. This had been reflected in nonresolution of postoperative hepatic insufficiency.

LATE RESULTS

Benign disease. The four patients recovered completely and have no complaints or hepatic function abnormalities after four to eight and one-half years (Table I).

Primary hepatic malignant lesion. The results are summarized in Table I. Of the 19 patients, 12 or 63 per cent are alive with follow-up periods of two months to five and one-half years. The six late deaths occurred two to 47 months postoperatively (Table I). All of the late deaths were caused by, or contributed to by, recurrent malignant tumor.

A better idea of the tumor control rate was ob-

tained by analyzing the 13 patients treated a year or longer ago for a primary hepatic malignant growth (Tables I and III). A tumor-free state at one year connoted a favorable prognosis for long term subsequent survival. Six of the 13 patients are dead. Three died after two, four and one-half and 12 months. Although the other three patients were alive for 19, 33 and 47 months, the presence of metastases was known by the end of the first postoperative year in all but the patient who survived for 33 months. Seven of the 13 patients are still alive. Six of these seven patients have no evidence of recurrence after follow-up periods of 66, 47, 42, 41, 21 and 13 months. The seventh patient is alive with metastatic hepatoma which was diagnosed one year postoperatively and which has been responsive to adriamycin therapy.

Foster (9) and others have noted that the long term results from hepatectomy are better in children than in adults. The breakdown of pediatric versus adult patients treated a year or longer ago for a primary hepatic malignant condition is given in Table III. Five of six children are still alive, and four are tumor-free after follow-up periods of three and one-half to five and one-half years. All six were given postoperative chemotherapy with agents summarized in Table IV for these as well as other pediatric patients. In contrast, only two of seven adults treated a year or longer ago are still alive and tumor-free but with shorter follow-up periods. The administration of

TABLE III.—ADULTS VERSUS CHILDREN, PRIMARY MALIGNANT CONDITIONS TREATED ONE YEAR OR LONGER WITH FOLLOW-UP STUDY TO 1 APRIL, 1979.

<i>Patients</i>	<i>No.</i>	<i>Dead</i>	<i>Alive with tumor</i>	<i>Alive, tumor-free</i>
Pediatric	6*	1 (19)	1 (21)	4 (66, 47, 42, 41)
Adult	7†			
No adjuvant therapy . . .	4	2 (2, 33)	0	2 (13, 21)
Adjuvant therapy . . .	3	3 (4½, 12, 47)	0	0

*Four hepatomas and two sarcomas. All had chemotherapy.

†Four hepatomas, one sarcoma, one cholangiocarcinoma and one squamous carcinoma in a cyst.

Figures in parentheses are months.

chemotherapy to the adults did not seem to have an effect on the outcome (Table III).

Metastases. Two of the seven patients with localized hepatic metastases are clinically tumor-free after nine and 52 months (Table II). The former is an adult and the latter a child. Two more are alive with metastases, one patient after six and the other after 41 months (Table II). This last patient had an abdominoperineal resection 18 months before hepatic trisegmentectomy. Eight months after hepatic resection, the right lower lobe of the lung was removed for localized metastases.

As with primary hepatic tumors, the presence or absence of tumor was usually apparent at one year. Recurrence did not preclude long term survival.

DISCUSSION

The general use of trisegmentectomy was discouraged by the high mortality recorded by Brunschwig (3) and others in an earlier time. As a consequence, large series were not reported except by Pack and associates (21) including Miller

TABLE IV.—TRISEGMENTECTOMY IN CHILDREN WITH FOLLOW-UP STUDY TO 1 APRIL, 1979

<i>Age</i>	<i>Diagnosis</i>	<i>Survival</i>	<i>Adjuvant therapy</i>
16	Adenoma	50 mos.	None
9	Hepatoma	66 mos.	Cytosin, vincristine, 5-FU‡
5	Hepatoma	Died 19 mos.*	Cytosin, vincristine, 5-FU
2	Neuroblastoma	52 mos.	Cytosin, vincristine, CCNU§, adriamycin, 3,100 rads
12	Sarcoma, ?	47 mos.	Cytosin, vincristine, 5-FU
12	Sarcoma	42 mos.	Cytosin, vincristine, actinomycin, DTIC , adriamycin
7	Hepatoma	41 mos.	Cytosin, vincristine, 5-FU
15	Hepatoma	21 mos.†	Cytosin, vincristine, 5-FU, adriamycin
15	Hepatoma	3 mos.	Cytosin, vincristine, 5-FU, adriamycin

*Massive recurrence.

†Lung metastases, responsive to adriamycin.

‡5-FU, 5-Fluorouracil.

§CCNU, Chloroethyl-cyclohexyl-nitrosourea.

||DTIC, Dacarbazine.

(18) at the Sloan-Kettering Institute, New York. They had acquired experience with 42 trisegmentectomies by the early 1970's. The largest recent collection was also reported from the same institution by Fortner and co-authors (7) who had reduced the mortality to 14.2 per cent in a more recent series consisting of 22 patients. However, the potential dangers of the procedure were emphasized by the 38 per cent mortality in 13 instances described by Almersjö and colleagues (1), as recently as 1976. Hemorrhage was the main cause of death.

The experience recorded herein establishes that right trisegmentectomy can be performed safely. The operative mortality was 3.3 per cent in a series of 30 patients that included many highly unfavorable lesions and older patients. Special hepatic compression clamps were not used, since they limit the extent of resection, nor were the isolation and perfusion techniques previously used by Fortner and associates (7) but subsequently abandoned by them (8).

The only operative death in our series was caused, at least partly, by postoperative thrombosis of a celiac axis that had been studied with selective angiography before surgical operation. This complication, as well as other less serious ones, has dampened our previously expressed enthusiasm (23) for preoperative arteriography. We still obtain such studies in about 20 per cent of the candidates for liver resection but only to answer specific questions of tumor localization not resolved by noninvasive methods, such as ultrasonography and computerized axial tomography.

The safety of right trisegmentectomy has made it reasonable to use this procedure to treat non-malignant lesions, such as giant adenomas. However, the question of its effectiveness in controlling malignant tumors still remains. The results so far have been encouraging.

More than 50 per cent of the patients with primary hepatic malignant growths were thought to be free of tumor after one year, and of these, only one patient subsequently had metastases develop. The good prognostic implication of a one year tumor-free state has been noted by Foster (9) and Lin (15) after less extensive resections. The one year follow-up period was equally decisive in patients with localized liver metastases. The early and late control rate after trisegmentectomy for metastases was somewhat less than that reported by Foster (10) and Wilson and Adson (28) in patients with generally less advanced and consequently less radically resected hepatic metastases.

The role, if any, of adjuvant chemotherapy and local irradiation in these results could not be determined. The tumors were wide ranging in cell type. The adjuvant treatment varied in its timing and consistency. Finally, the numbers of untreated potential control patients were small and too often selected out for nontreatment by advanced age or infirmity. Long term survival was obtained without, as well as with, chemotherapy.

Nevertheless, a case for adjuvant chemotherapy can be made. As reviewed by Foster (9) and Lee (14), hepatomas and other primary hepatic tumors were considered, until recently, to be non-responsive to antitumor drugs. The results of recent reports have been less pessimistic about individual and multiple agents. Moertel (19) and Kennedy and associates (13) reported that a significant number of patients with nonresectable hepatomas responded to 5-fluorouracil, a claim not supported by Link and co-workers (16) and numerous earlier workers. In contrast, adriamycin has been said to be variably effective for surgically untreatable hepatomas by Olweny (20), Ihde (12), Vogel (26) and Baker (2) and their associates. In the study done by Olweny and colleagues (20), the results in a Ugandan population were better than those in the United States.

Treatment with cyclophosphamide, vincristine and 5-fluorouracil as an adjuvant to resection for hepatoblastoma was advocated by Holton and co-authors (11) in 1975. The treatment of many of our patients, of whom most had hepatomas, followed their protocol. Cochrane and associates (5) showed that such treatment plus methotrexate gave a survival advantage to patients with hepatoma for whom surgical resection was not possible; irradiation of the liver was of no value. The addition of adriamycin to the treatment of Holton (11) and Cochrane (5) and their co-workers should be considered in future patients. The concept that minimal residual disease can thereby be controlled after hepatic resection will have to be tested with rigid protocols and appropriate controls.

The possible value of multimodality therapy was particularly evident in the eight pediatric patients of our trisegmentectomy series. Seven are alive. The one death occurred after 19 months. Another patient who was operated upon 21 months ago has recurrences which are highly responsive to adriamycin treatment. Six of the eight patients are clinically tumor-free. Five of these six have follow-up periods of three and one-half

to five and one-half years; the trisegmentectomy in the sixth patient was done only three months ago.

SUMMARY

Thirty patients had right trisegmentectomy for 19 primary hepatic malignant tumors, seven localized liver metastases and four benign lesions. A technical refinement that aided resection of bulky posterior and superior tumors was intrahepatic identification and control of the right hepatic vein. The operative mortality was 3.3 per cent. Late hepatic insufficiency was not observed. More than one-half of the patients operated upon a year or more ago for primary hepatic malignant growths had a tumor-free state at the 12 month follow-up period. Beyond this time, there was only one recurrence. The results in children were twice as good as in adults. The results in treating localized liver metastases from distant primary sites were inferior to those in treating primary hepatic tumors. A hypothetical case was made for combining hepatic resection with adjuvant chemotherapy, even though our experience could not be construed as direct support for this practice.

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